SHORT REPORT

Clinicoradiological features of tuberculous meningitis in patients over 50 years of age

S G Srikanth, A B Taly, K Nagarajan, P N Jayakumar, S Patil

J Neurol Neurosurg Psychiatry 2007;**78**:536–538. doi: 10.1136/jnnp.2006.095620

Background and aim: Tuberculous meningitis (TBM) is a debilitating form of CNS tuberculosis with a high morbidity and mortality in spite of treatment. The diagnosis is based on clinical, radiological and laboratory features. The classical CT features of basal exudates, hydrocephalus, infarcts and granulomas have been mostly reported in younger individuals. Our aim was to study imaging features of TB meningitis in adults over the age of 50 years.

Materials and methods: Clinical, imaging and laboratory features of 53 adult patients over the age of 50 years (sixth to eighth decades) were studied retrospectively. Diagnosis of TBM was based on clinical and laboratory features.

Results: Imaging features were the conspicuous absence of typical features of TBM (ie, basal meningeal enhancement, hydrocephalus, infarcts/granulomas were seen in only a minority of patients).

Conclusions: CT features of TBM in elderly patients were few, atypical and non-contributory for diagnosis, probably because of age related immune senescence. Strong clinical suspicion and correlation with laboratory findings is necessary for early diagnosis.

The elderly population is increasing all over the world, including India, because of increased life expectancy. The incidence of tuberculosis has been estimated to be higher in elderly subjects than in younger populations.[1] Non-specific clinical symptoms may be masked by illnesses prevalent in old age, such as diabetes mellitus, vascular diseases and malignancies. CT has been used in the evaluation of tuberculous meningitis (TBM) to identify complications and for prognosis. CT features include basal meningeal enhancement, hydrocephalus, infarctions and focal granulomas.[2] We report a retrospective study of clinical and radiological features of TBM in patients over the age of 50 years (sixth to eighth decades).

MATERIAL AND METHODS

We retrospectively studied 53 patients over the age of 50 years (sixth to eighth decades) who presented with a diagnosis of TBM at the emergency services between January 2001 and May 2003 in a (single centre) tertiary level teaching hospital. The diagnostic criteria (see below) included clinical features and laboratory results. For the purpose of this study, the clinical and laboratory findings were correlated with CT findings. Patients were excluded if they did not meet the diagnostic criteria, were aged less than 50 years, had refused further medical management or were not investigated with CT.

The definite criterion used for a diagnosis of TBM was a positive culture or demonstration of mycobacterium by acid-fast stain. The probable criteria were the following: clinical features of fever, headache and altered sensorium; predominant lymphocytes ($>10/mm^3$) in CSF with high protein (>40 mg/dl) and low CSF/serum glucose ratios (<0.5); response to therapy; positive Mantoux reaction; contact history (eg, close family member); or past history of pulmonary TB. Analysis of clinical data and laboratory results were done by a neurologist and a microbiologist, respectively.

Both non-contrast and post-contrast CT studies were available for 40 patients whereas 13 patients had only post-contrast CT data. The CT studies were performed on a sequential scanner (Somatom, Siemens, Erlangen, Germany) with a protocol of 5 mm thick axial sections for the posterior fossa up to the basal cisterns and 8/10 mm in the supratentorial region up to the vault. The CT images were analysed by two neuroradiologists (one blinded to the clinical diagnosis) independent of the features of TB meningitis (presence of basal exudates, hydrocephalus, infarcts and granulomata). Hydrocephalus was considered obstructive if ventriculomegaly was associated with periventricular lucencies, effacement of sulci and rounding (ballooning) of frontal and temporal horns. Non-obstructive ventriculomegaly was graded as mild, moderate or severe. Age related changes in volume loss (both cortical and subcortical) were documented.

RESULTS

There were 53 patients (38 males and 15 females) aged 50–80 years (mean 59.7 (9.2) years). The major clinical presentations were: fever (n = 43), headache (n = 25), vomiting (n = 18), neck rigidity (n = 27), altered sensorium (n = 34), seizures (n = 15) and focal neurological deficits (n = 13). Evidence of pulmonary tuberculosis on chest radiography was noted in 18 patients (sputum was positive in 5 patients). CSF analysis revealed cell counts ranging from 0 to 600 cells/ml (predominantly lymphocytes 10–100%) with protein (range 10–466 mg/dl). CSF antituberculous antibody IgG was positive in 6 patients and culture was positive in 3 patients. Thus 8 patients fulfilled definite criteria and 45 patients fulfilled probable criteria for TBM. CSF analysis for HIV by western blot was available for 29 patients and was negative in all. Other associated risk factors such as chronic alcoholism and diabetes mellitus were noted in 13 and 9 patients, respectively.

The CT findings were conspicuous by their absence (fig 1). Basal meningeal enhancement was seen in only two patients. Ventriculomegaly was observed in 23 patients (mild in 16, moderate in 6 and severe in 1). Periventricular lucency was noted in 7 patients with moderate and severe ventriculomegaly. Non-enhancing hypodensity due to infarction was noted in only 2 patients (basal ganglia and frontal lobe, respectively) and enhancing lesions suggestive of granulomas were seen in 4 patients. There was no discordance between the neuroradiologists regarding the findings.

DISCUSSION

TBM is common in developing countries, with a high morbidity and mortality. The diagnosis of TBM is based mainly on clinical and laboratory findings, particularly in adults.[3] As the prognosis

Abbreviation: TBM, tuberculous meningitis

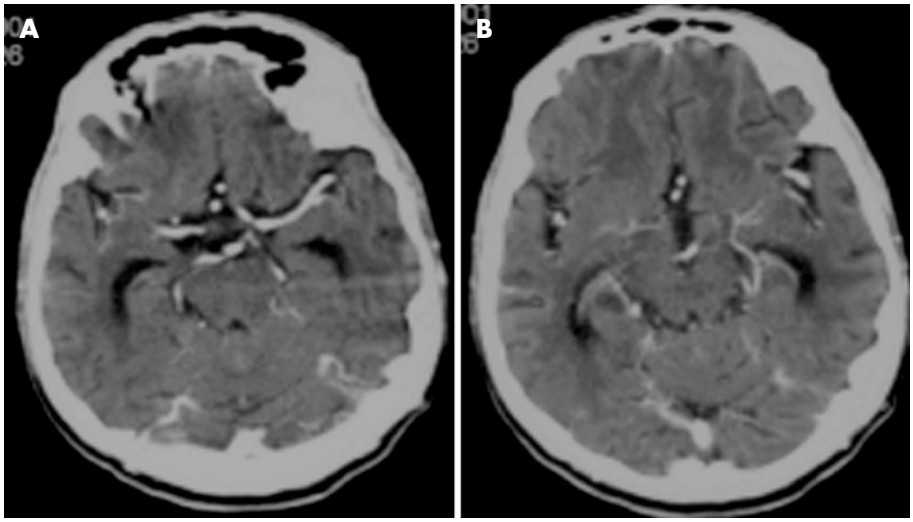

Figure 1 (A, B). Plain and contrast CT of a 63-year-old man at the level of the basal cisterns showing absence of any enhancing exudates in the cisterns. Mild dilatation of the temporal horns and third ventricle are noted.

depends on starting treatment early, and confirmatory tests take longer time (culture) or are not available (PCR) in regions where tuberculosis is common, the diagnosis is based on clinical, laboratory and imaging features.

CT and MRI are used in the evaluation of TBM and to identify complications. Typical imaging features include meningeal enhancement, hydrocephalus, parenchymal granulomata and infarcts.[2] Pathological features in TBM are mainly caused by the presence of dense fibrinous exudate in the basal subarachnoid spaces.[4] Formation of exudates requires a competent immune system in the host. Cell mediated immunity plays a major role and many pathological features of TBM are the result of hypersensitivity immune responses to the mycobacterium in the subarachnoid space.[5] Tuberculosis in the elderly is usually the result of reactivation of latent infection.[6] The immune system also undergoes age related changes as people get older. The increased prevalence of infection, neoplasia and autoantibodies with ageing may in turn cause changes in the immune system. In addition, protein energy malnutrition and deficiency of zinc, selenium and pyridoxine prevalent in the elderly population may have a similar effect on the immune system.[7] Imaging features in our elderly patients were different from those with an intact immune system reported in the literature and rather resembled those patients with HIV infection. Basal meningeal enhancement was noted in only 2 (3.3%) patients in our group compared with reported values of approximately 60% of cases. Hydrocephalus was found in 7 patients compared with reported values of approximately 50–80%. Infarction was seen in only 2 (3.3%) patients whereas in the literature it was seen in about 28–40% of TBM cases.[2] Fewer imaging findings in our patients were probably due to absence or smaller amounts of exudate in the basal cisterns. Age related changes in cell mediated immunity and decreased humoral responses to antigenic stimuli in the elderly might be the cause of the minimal amounts of exudate resulting in such atypical, minimal imaging findings. Clinical, radiological and pathological features of TBM in patients with and without HIV have been compared. Sarosh *et al*[8] found minimal meningeal enhancement on CT scan and scant exudates on pathology in TBM patients associated with HIV infection compared with those without HIV infection (table 1). In addition, obstructive hydrocephalus and parenchymal granulomas were conspicuously minimal or absent in patients with HIV infection. Absence of significant exudates in the basal cisterns explains the paucity of imaging features of TBM.

Table 1 Comparison of imaging features of tuberculous meningitis in HIV positive and HIV negative patients, and in the present study

	Sarosh *et al*[8] HIV+ve	Sarosh *et al*[8] HIV−ve	Present study
No of patients	18	22	53
Basal exudates (%)	33.3	81	3.8
Hydrocephalus (%)	5.5	63.6	13.1
Infarcts (%)	38.9	40.9	3.8
Granuloma (%)	33.3	22.7	7.6
Cerebral atrophy (%)	44.4	4.5	23

Although it might be argued that MRI may have added more findings in such patients, studies comparing CT and magnetic resonance have shown that the difference is minimal in terms of hydrocephalus and basal exudates.[9] Magnetic resonance has shown superiority in delineating infarcts (both ischemic and haemorrhagic) and cranial nerve enhancement. The presence of hydrocephalus has prognostic implications[10] and it was seen in a few (13.1%) of our patients in this study.

Previous studies have shown that demonstration of mycobacterium ex vivo or in culture, albeit the gold standard for diagnosis, is time consuming and not positive in all cases. Antituberculous treatment needs to be initiated on clinical suspicion, and laboratory (CSF) and imaging findings. However, there are currently no pathognomonic imaging correlates to validate a clinical impression of infection and the imaging features are, at best, corroborative. Also, features suggestive of infection, if any, may be undermined or made less apparent by the age related changes in elderly patients. The aim of the current study was to highlight the paucity of imaging findings that can delay treatment in the potentially early stage. Although our study has the limitations inherent in any retrospective study, we believe the findings warrant a more structured prospective study to confirm the relative paucity of CT features in TBM in the elderly. Further studies may suggest appropriate modification of current diagnostic and management guidelines of TBM in this vulnerable age group.

CONCLUSIONS

Imaging features of TBM in the elderly are atypical because of minimal or absence of basal exudates, probably secondary to age related immune senescence. Strong clinical suspicion and correlation with laboratory investigations are essential for the early diagnosis of TBM in elderly individuals.

ACKNOWLEDGEMENTS

Our sincere and profound gratitude to Dr SK Shankar MD, Professor and Head, Department of Neuropathology, NIMHANS, for his valuable comments and suggestions on the final manuscript.

Authors' affiliations

S G Srikanth, K Nagarajan, P N Jayakumar, Department of Neuroimaging and Interventional Radiology, National Institute of Mental Health and Neurosciences, Bangalore, India
A B Taly, Department of Neurology, National Institute of Mental Health and Neurosciences, Bangalore, India
S Patil, Department of Neuromicrobiology, National Institute of Mental Health and Neurosciences, Bangalore, India

Competing interests: None declared.

Correspondence to: Dr S G Srikanth, Department of Neuroimaging and Interventional Radiology, National Institute of Mental Health and Neurosciences, Bangalore 560029, India; sgsrikanth@yahoo.com

Received 21 April 2006
Revised 11 December 2006
Accepted 21 December 2006
Published Online First 12 January 2006

REFERENCES

1 **Powell KE**, Farer LS. The rising age of tuberculosis patients: a sign of success and failure. *J Infect Dis* 1980;**142**:946–8.
2 **de Castro CC**, de Barros NG, Campos ZM, *et al*. CT scans of cranial tuberculosis. *Radiol Clin North Am* 1995;**33**:753–69.
3 **Thwaites GE**, Chau TTH, Stepniewska K, *et al*. Diagnosis of adult tuberculous meningitis by use of clinical and laboratory features. *Lancet* 2002;**360**:1287–92.
4 **Lurie MB**. *Resistance to tuberculosis: experimental studies in native and acquired defensive mechanisms*. Cambridge: Harvard University Press, 1964.
5 **Rich AR**, McCordock HA. Pathogenesis of tuberculous meningitis. *Bull John Hopkins Hosp* 1933;**52**:5–37.
6 **Dutt AK**, Stead WW. Tuberculosis in the elderly. *Med Clin North Am* 1993;**77**:1353–68.
7 **Lesourd BM**. Nutrition and immunity in elderly; modification of immune responses with nutritional treatment. *Am J Clin Nutr* 1997;**66**:478S–84.
8 **Sarosh MK**, Prafulla KS, Sanjay R, *et al*. The clinical, radiological and pathological profile of tuberculous meningitis in patients with and without HIV infection. *J Neurol Sci* 2000;**181**:118–26.
9 **Chang KH**, Han MH, Roh JK, *et al*. Gd-DTPA enhanced MR imaging in intracranial tuberculosis. *Neuroradiology* 1990;**32**:19–25.
10 **Chan KH**, Cheung RTF, Fong CY, *et al*. Clinical relevance of hydrocephalus as a presenting feature of tuberculous meningitis. *Q J Med* 2003;**96**:643–8.